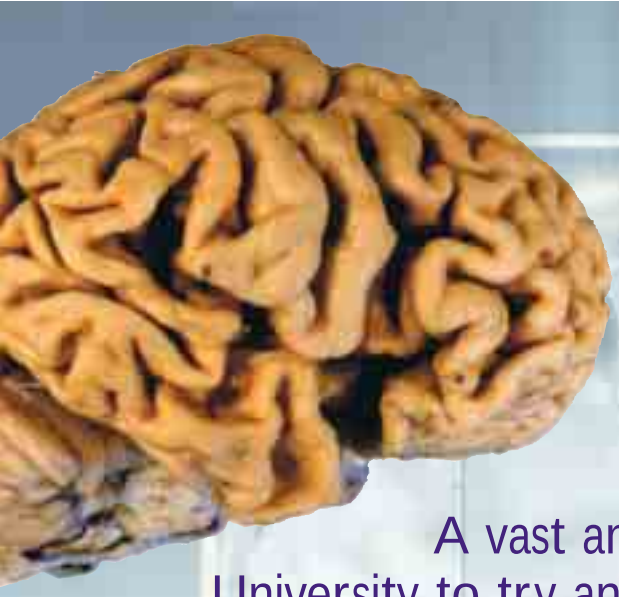


Photo: Seth Love

Bristol and the Brain

A vast amount of research is being done at Bristol University to try and understand the workings of the brain – from the functioning of cells through to experimental psychology. Over the next few issues of *re:search*, a series of articles will review the wide range and diversity of this work.

NEUROSCIENCE: REPAIR AND REGENERATION

Only 30 years ago, neuroscience barely existed as a separate discipline. Today, it is one of the most exciting areas of biomedical research. Startling discoveries have transformed our understanding of the healthy brain and helped to deliver treatments for disorders affecting millions of people.

Bristol University's Institute of Clinical Neurosciences (ICN) was established in late 1999. Based at Frenchay Hospital in north Bristol, the Institute was a joint venture between the University of Bristol, the (then) Frenchay NHS Trust and the Burden Neurological Institute. It is the principal integrated clinical neuroscience unit in the south west. Collectively the various core component groups are pursuing three themes relating to neurological disease and disability – understanding disease, limiting damage and promoting repair.

Neuroscience is the study of the nervous system – the brain, the spinal cord and the networks of sensory nerve cells, or neurons, throughout the body. Humans contain roughly 100 billion neurons, the functional units of the nervous system. Neurons communicate with each other by sending out electrical signals and then releasing chemicals called neurotransmitters which cross synapses – the small gaps between neurons.

Neuroscience research encompasses thousands of diseases and disorders from drug addiction to Alzheimer's, as well as the study of brain development, sensation and perception, learning and memory, movement, sleep, stress, ageing and neurological and psychiatric disorders. It also includes the molecules, cells and genes responsible for nervous-system functioning. Research in neuroscience advances the understanding of human thought, emotion and behaviour.

Neuroscientists use tools ranging from computers to special dyes to examine molecules, nerve cells, networks, brain systems, and behaviour. From these studies they learn how the nervous system develops and functions normally and what goes wrong in neurological disorders. Increasingly, therefore, it is in the realm of promoting repair where greatest effort is concentrated. This is powerfully illustrated by the enormously exciting clinical experimental therapeutic neurosurgery programme run by Mr Steven Gill.

Adult human neural stem cells

> Given the choice, most of us would rather not have a hole drilled in the skull

Given the choice, most of us would rather receive medicine through an injection into the blood stream than have a hole drilled in the skull. Unfortunately, many of the new therapies developed for brain ailments cannot be administered through the blood because the body bars them from crossing into the brain. This blood-brain barrier prevents many things that make it into the blood stream, such as toxins, from tainting the brain's pristine nerve cell habitat.

Gill's work with Parkinson's disease patients involves the insertion of an ultra-thin catheter into the region of the brain which is deficient in dopamine. Without dopamine, the nerve cells cannot properly transmit messages to the body which results in the deterioration of movement seen in people with Parkinson's disease. The catheters are connected to pumps filled with glial derived neurotrophic ➜

➜ factor (GDNF), which continuously infuse the growth factor to this area of the brain. GDNF is a natural growth factor required for the development, guidance and maintenance of nerve cells that produce dopamine.

Pilot studies on five people have produced "astonishing" results, with marked improvement in symptoms shown by all patients. This pioneering work is at the forefront of international therapeutic neuroscience but the treatment is in its infancy and multiple further trials are needed to asses its safety and longer-term efficacy. The work is continuing and there are plans for similar techniques to be applied to patients with other neurodegenerative diseases, particularly Alzheimer's.

Pilot studies on five people have produced "astonishing" results

The most recent group to become established on the Frenchay campus is centred on the clinical and biological problems posed by multiple sclerosis and other inflammatory diseases. This work is the particular interest of Neil Scolding, Burden Professor of Clinical Neuro-sciences, and Director of the Institute.

Multiple sclerosis (MS) is most frequently diagnosed in young adults in their mid-twenties to mid-thirties. It is a common cause of chronic neurological disability in this age group, affecting approximately 85,000 people in the UK. In most people it is characterised by muscle weakness, loss of co-ordination and sensory problems, and alternating periods of relapse and remission.

In the brain and spinal cord, thin fibres called axons – elongated extensions of neurons – transfer signals backwards and forwards to target cells. Each axon is surrounded by a fatty sheath of myelin. The cause of MS is still unknown, but the problems are due to patchy destruction of the myelin and the brain cells – *oligodendrocytes* – responsible for making and maintaining it. When this insulating sheath is destroyed the myelin is replaced by scar-like tissue and nerve signalling is blocked, so the neurons no longer pass messages to one another efficiently, resulting in the impairments of limb and eye movement, vision, sensation and balance that characterise multiple sclerosis. It is now clear that the brain has a capacity, albeit limited, for repairing myelin sheaths and restoring function. This has only been realised in the last decade or so, despite the fact that MS has been studied for over a century. It immediately begs a number of exciting and important questions. First, why is it that some areas repair well, others only very poorly? Second, and most important, can ways be developed of promoting myelin repair in patients?

Professor Scolding has established a programme of research designed to study the biology of myelin repair in multiple sclerosis. Simultaneous clinical research is intended to establish and validate a framework protocol for implementing therapeutic myelin repair strategies in patients. New treatments, designed to prevent the progression of disability, may offer the hope that some restoration of function in previously damaged areas of the brain or spinal cord might be stimulated.

Professor Scolding's group has recently identified a cell in the human brain which is likely to be responsible for carrying out myelin repair and they now routinely grow and study such cells in the test tube. In the Glial Cell Laboratories on the Frenchay site, they are exploring in detail the behaviour of these cells and in particular their ability to make myelin; they are also studying other human nerve cell types which are related to *oligodendrocytes* in that they too can make myelin sheaths.

Investigations will explore whether these cell types might be suitable for the development of new treatments aimed at supplementing myelin repair in patients, probably by cell transplantation. Scolding believes that such treatments will be ready for preliminary clinical experimental trials within the next few years, which he aims to conduct at Frenchay, again in collaboration with Steven Gill.

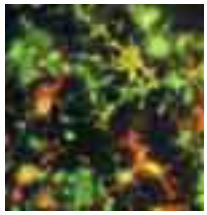
In addition to myelin repair and regeneration, Scolding is also involved in a number of clinical therapeutic trials attempting to reduce tissue damage and slow down the progression of disease. This work builds on pioneering immunological research by the University's Professor David Wraith. He has shown in laboratory studies that it is possible to "re-educate" the immune system, preventing it from continuing to cause further damage to the brain and spinal cord. Scolding and Wraith hope that this therapy can be translated into clinical trials in MS patients within the next 12 months.

Plans to build a *Centre for Multiple Sclerosis* on the Frenchay site are already well under way. Patients will be seen and cared for, clinical treatment trials in MS conducted and new research carried out all within the same facility. Approximately £750, 000 has been raised towards the target of £1.25m by the dedicated MS charity, the MS Nerve Centre, whose fundraising is now based at Frenchay. The Centre will be a unique development in MS in this country. ■

www.bris.ac.uk/Depts/DivMed

Photos: Neil Scolding

Axons and myelin



Human brain cells